



A 25-year follow-up of patients admitted to methadone treatment for the first time: Mortality and gender differences

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ABSTRACT

Introduction: We conducted a follow-up study to evaluate the outcome of a heroin-dependent population 25 years after their first enrollment in methadone maintenance treatment (MMT). We assessed mortality in the sample plus actual drug use, treatment, and medical factors associated with drug dependence, focusing on possible gender differences.

Methods: Prospective follow-up study of 214 heroin-dependent patients consecutively admitted for MMT between 1980 and 1984 in the Asturias Public Health Service. The standardized mortality ratio (SMR) and 95% confidence interval (CI) were calculated. An ad-hoc protocol on drug misuse and treatment, drug-related morbidity and Clinical Global Impression (CGI) scores were assessed in the survivors' sample.

Results: Information was received on 159 subjects, 106 of whom were deceased. Men accounted for 76.2% of the study cohort. Over the 25-year follow-up period, the SMR was 22.51 (95% CI = 22.37–22.64). In the survivors sample, 39.6% were still enrolled in MMT; human immunodeficiency virus (HIV) was diagnosed in 47.2% and hepatitis B/C in 81.1%; current heroin use was reported by 22.6%. There were no gender differences in mortality or HIV and hepatitis B/C status. None of the female survivors were using heroin at the 25-year follow-up compared with 31.1% of males.

Conclusions: This study confirms the high mortality of heroin addicts even after enrollment in MMT. Severity of the addiction in terms of mortality was similar in both genders. Women who survived the 25-year follow-up were more likely to have stopped using heroin than men.

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1. Introduction

Heroin addiction has often been characterized as a chronic relapsing condition, and for many addicts, it is a persistent, long-term affliction with severe consequences, particularly in terms of premature mortality and high morbidity (Hser, Hoffman, Grella, & Anglin, 2001).

One of the principal treatments for heroin dependence in many countries is methadone maintenance treatment (MMT) (Hall, Lynskey, & Degenhardt, 2000) with an estimated 1 million individuals receiving MMT worldwide (Kleber, 2008).

Numerous studies have demonstrated the effectiveness of MMT for reducing illicit opioid use, morbidity and mortality, risk of human

immunodeficiency virus (HIV) infection, and illegal activities, and for improving overall functioning (Kleber, 2008).

Patients in MMT have a 1-year mortality rate of 1% (Zanis & Woody, 1998) while a number of studies have suggested that the annual death rate of young adult drug abusers lies at around 2% to 8% per year (Haastrop & Jepsen, 1988; Oppenheimer, Tobutt, Taylor, & Andrew, 1994; Ravndal & Vaglum, 1998; Segest, Mygind, & Bay, 1990; Zanis & Woody, 1998).

The benefits of long-term MMT are borne out by the data (National Institutes of Health, 1997). In randomized controlled trials and controlled observational studies, MMT has been shown to result in substantial reductions in illicit opioid use and criminal activity (Ward, Mattick, & Hall, 1998) and to substantially reduce opioid overdose deaths while individuals are enrolled in MMT (Coplehorn, Dalton, Cluff, & Petrenas, 1994; Coplehorn, Dalton, Haldar, Petrenas, & Nisbet, 1996; Gearing & Schweitzer, 1974; Zador, Sunjic, & Basili,

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1998), although a considerable number of deaths still occur in patients on maintenance treatment, including many taking methadone (Heinemann, Iwersen-Bergmann, Stein, Schmoldt, & Püschel, 2000; Mattick & Degenhardt, 2003). Although MMT has been lifesaving for thousands of individuals, it is not a panacea. High levels of psychopathology remain. Abuse of cocaine and benzodiazepines and disruptive behavior are problems in many programs. Many patients do not change their behavior even when services are available (Kleber, 2008).

Generally, transition to abstinence is highest in the first few years that substance abusers are treated, but few become abstinent after the first few years (Haastrup & Jepsen, 1988; Hser et al., 2001; Hubbard, Craddock, & Anderson, 2003). Even patients receiving maintenance for long periods with substantial lifestyle changes often relapse after leaving treatment, and death rates are much higher than for individuals who remain in treatment. For many patients, therefore, years or even lifetime maintenance may be needed (Kleber, 2008).

Relatively little is known about long-term recovery processes among addicts who do achieve and maintain abstinence, as there are few long-term follow-up studies on this type of patients (see Table 1). This might be related to the difficulty of tracking substance abusers in longitudinal research (Jimenez et al., 2000; Walton, Ramanathan, & Reischl, 1998).

Although drug overdose is the leading cause of death in most long-term follow-up studies on opioid dependence (Bauer et al., 2008; Goldstein & Herrera, 1995; Haastrup & Jepsen, 1988; Hall et al., 2000; Hser et al., 2001; Nehkant, Rathod, Addenbrooke, & Rosenbach, 2005; Oppenheimer et al., 1994), somatic comorbidities, such as HIV infection, were also associated with an increased mortality rate prior to the introduction of potent antiretroviral therapies in the mid-1990s (Muga et al., 2000). AIDS is a leading cause of death among injection drug users, and serious infections resulting in pneumonia, endocarditis, and sepsis are also responsible for high death rates among this subpopulation (Tyndall et al., 2001). Additionally, hepatitis C infections and nonalcoholic liver disease have been shown to negatively influence death rates (Appel, Joseph, & Richman, 2000).

The excess mortality over the life-span of drug abusers is of interest, because it implies the need for services over the life course, over and above the need for treatment services that show effectiveness in the short term (Fridell & Hesse, 2006).

The recent focus on drug abuse in women has brought attention to numerous differences between women and men (Lynch, Roth, & Carroll, 2002). Sex differences are present for all phases of drug abuse (initiation, escalation of use, addiction, and relapse following abstinence). Females begin regularly self-administering licit and illicit drugs of abuse at lower doses than do males, use escalates more rapidly to addiction, and females are at greater risk for relapse following abstinence (Becker & Hu, 2008). Clinical studies report outstanding differences with regard to substance misuse patterns,

social support and evolution of the treatment according to the gender (either male or female). Men have better prognosis than women in the population studied. These differences seem to be due to the sociocultural contents of the gender concept (Ochoa, Madoz-Gúrpide, & Salvador, 2008).

Recent evidence suggests that the progression to dependence and abuse may differ between women and men; thus, different prevention and treatment strategies may be required. (Lynch et al., 2002). These gender differences in addictive behaviors have been explained by sociocultural as well as biological factors (Becker & Hu, 2008; Lynch et al., 2002).

Despite the evidence of gender differences in drug dependence, there is a lack of data from long-term follow-up studies concerning possible gender differences in death/survival rates. The few existing data suggest a higher mortality rate among men (Bauer et al., 2008; Coffin et al., 2003; Fridell & Hesse, 2006; Hickman et al., 2003).

The aim of our work is to evaluate the outcome of a heroin-dependent population 25 years after their first enrollment in MMT, focusing on gender differences. More specifically, we evaluate excess mortality by gender, plus current drug misuse and treatment, drug related morbidity, and clinical global impression in the survivors.

2. Material and methods

2.1. Participants and setting

The study was conducted prospectively on a sample of 214 heroin-dependent patients consecutively admitted for MMT between 1980 and 1984 to different health facilities in the Asturias Public Health Service. They were the first patients to be enrolled in MMT in Asturias. The first interview took place at the time of enrollment in MMT. Data were collected by means of an ad-hoc protocol on drug dependence, including sociodemographic, clinical, family, job, and legal data. All subjects who presented for treatment were entered in the sample even if they left treatment prematurely.

2.2. Follow-up procedure

At the 15-year follow-up, patients were contacted by telephone. Data were collected by telephone interviews and/or review of medical records. The main findings from the 15-year follow-up are reported elsewhere (Jimenez et al., 2000).

The 25-year follow-up is the main subject of the present work. Prior to the assessment, we have made an extensive effort to locate the patients. Patients were invited to participate in the study in a telephone interview by members of the research team or in a personal interview by their regular health care provider.

Assessment interviews were done by a trained research psychologist. Personal interviews were preferred for the assessment, but telephone

Table 1
Mortality in heroin-dependent population in follow-up studies.

Study (year)	Country	Duration of follow-up (years)	Deaths%	Sample size and derivation
Bauer et al. (2008)	Austria	5	25.4	269 opioid-dependents enrolled in MMT
Sanchez-Carbonell and Seus (2000)	Spain	10.5	30	138 heroin addicts admitted for the first time to EMETYST Project
Fridell and Hesse (2006)	Sweden	15	24	125 drug abusers admitted for detoxification at Sankt Lars Hospital
Davstad et al. (2009)	Sweden	18	45	157 heroin-dependent subjects admitted for the first time to MMT in Stockholm
Vaillant (1973)	USA	20	23	100 people with narcotic addiction admitted to Lexington Hospital, NY
Oppenheimer et al. (1994)	UK	22	34	128 patients from 13 drug dependency clinics in London
Jimenez-Treviño et al. (present study)	Spain	25	49.5	214 heroin dependents admitted for the first time to MMT
Hser et al. (2001)	USA	33	48.9	581 white men admitted to California Drug Addiction Program
Nehkant et al. (2005)	UK	33	22	86 heroin dependents seen for therapeutic intervention
Stenbacka et al. (2010)	Sweden	37	50.4	1705 substance abusers identified through medical records in Stockholm

MMT = methadone maintenance treatment.

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